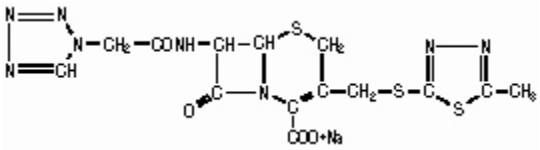
ANCEF - cefazolin sodium injection
GlaxoSmithKline

DESCRIPTION

ANCEF is a semi-synthetic cephalosporin for parenteral administration. It is the sodium salt of 3-{[(5-methyl-1,3,4-thiadiazol-2-yl)thio]-methyl}-8-oxo-7-[2-(1H-tetrazol-1-yl)acetamido]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid.
Structural Formula:



Each vial contains 48 mg of sodium/1 gram of cefazolin sodium.
ANCEF in lyophilized form is supplied in vials equivalent to 1 gram of cefazolin; in “Piggyback” Vials for intravenous admixture equivalent to 1 gram of cefazolin; and in Pharmacy Bulk Vials equivalent to 10 grams of cefazolin.

CLINICAL PHARMACOLOGY

After intramuscular administration of ANCEF to normal volunteers, the mean serum concentrations were 37 mcg/mL at 1 hour and 3 mcg/mL at 8 hours following a 500-mg dose, and 64 mcg/mL at 1 hour and 7 mcg/mL at 8 hours following a 1-gram dose.
Studies have shown that following intravenous administration of ANCEF to normal volunteers, mean serum concentrations peaked at approximately 185 mcg/mL and were approximately 4 mcg/mL at 8 hours for a 1-gram dose.
The serum half-life for ANCEF is approximately 1.8 hours following IV administration and approximately 2.0 hours following IM administration.
In a study (using normal volunteers) of constant intravenous infusion with dosages of 3.5 mg/kg for 1 hour (approximately 250 mg) and 1.5 mg/kg the next 2 hours (approximately 100 mg), ANCEF produced a steady serum level at the third hour of approximately 28 mcg/mL.
Studies in patients hospitalized with infections indicate that ANCEF produces mean peak serum levels approximately equivalent to those seen in normal volunteers.
Bile levels in patients without obstructive biliary disease can reach or exceed serum levels by up to 5 times; however, in patients with obstructive biliary disease, bile levels of ANCEF are considerably lower than serum levels (<1.0 mcg/mL).
In synovial fluid, the level of ANCEF becomes comparable to that reached in serum at about 4 hours after drug administration.
Studies of cord blood show prompt transfer of ANCEF across the placenta. ANCEF is present in very low concentrations in the milk of nursing mothers.
ANCEF is excreted unchanged in the urine. In the first 6 hours approximately 60% of the drug is excreted in the urine and this increases to 70% to 80% within 24 hours. ANCEF achieves peak urine concentrations of approximately 2,400 mcg/mL and 4,000 mcg/mL respectively following 500-mg and 1-gram intramuscular doses.
In patients undergoing peritoneal dialysis (2 L/hr.), ANCEF produced mean serum levels of approximately 10 and 30 mcg/mL after 24 hours’ instillation of a dialyzing solution containing 50 mg/L and 150 mg/L, respectively. Mean peak levels were 29 mcg/mL (range 13 to 44 mcg/mL) with 50 mg/L (3 patients), and 72 mcg/mL (range 26 to 142 mcg/mL) with 150 mg/L (6 patients).
Intraperitoneal administration of ANCEF is usually well tolerated.
Controlled studies on adult normal volunteers, receiving 1 gram 4 times a day for 10 days, monitoring CBC, SGOT, SGPT, bilirubin, alkaline phosphatase, BUN, creatinine, and urinalysis, indicated no clinically significant changes attributed to ANCEF.

Microbiology

In vitro tests demonstrate that the bactericidal action of cephalosporins results from inhibition of cell wall synthesis. Cefazolin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections as described in INDICATIONS AND USAGE.

Gram-Positive Aerobes

Staphylococcus aureus (including β-lactamase–producing strains)

Staphylococcus epidermidis

Streptococcus pyogenes,Streptococcus agalactiae, and other strains of streptococci

Streptococcus pneumoniae

Methicillin-resistant staphylococci are uniformly resistant to cefazolin, and many strains of enterococci are resistant.

Gram-Negative Aerobes

Escherichia coli

Proteus mirabilis

Most strains of indole positive Proteus (*Proteus vulgaris*), *Enterobacter* spp., *Morganella morganii*, *Providencia rettgeri*,*Serratia* spp., and *Pseudomonas* spp. are resistant to cefazolin.

Susceptibility Tests

Diffusion Techniques
Quantitative methods that require measurement of zone diameters provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure[1] that has been recommended for use with disks to test the susceptibility of microorganisms to cefazolin uses the 30-mcg cefazolin disk. Results of the standardized single-disk susceptibility test[1] with a 30-mcg cefazolin disk should be interpreted according to the following criteria:

RECOMMENDED RANGES FOR CEFAZOLIN SUSCEPTIBILITY TESTING

Zone Diameter (mm)	Interpretation
≥18	Susceptible (S)
15-17	Intermediate (I)
≤14	Resistant (R)

Standardized single-disk susceptibility test should be performed ONLY with a 30-mcg cefazolin disk.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited by usually achievable concentrations of the antimicrobial compound in the blood. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that usually achievable concentrations of the antimicrobial compound in the blood are unlikely to be inhibitory and that other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory control microorganisms. The 30-mcg cefazolin disk should provide the following zone diameters in these laboratory test quality control strains:

Microorganism		Zone Diameter (mm)
E. coli	ATCC 25922	21-27
S. aureus	ATCC 25923	29-35

The cefazolin disk should not be used for testing susceptibility to other cephalosporins.

Dilution Techniques
Quantitative methods that are used to determine minimum inhibitory concentrations provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure uses a standardized dilution method[2] (broth, agar, or microdilution) or equivalent with cefazolin powder. The MIC values obtained should be interpreted according to the following criteria:

MIC (mcg/mL)	Interpretation
≤16	Susceptible (S)
≥64	Resistant (R)

Interpretation should be as stated above for results using diffusion techniques.

As with standard diffusion techniques, dilution methods require the use of laboratory control microorganisms. Standard cefazolin powder should provide the following MIC values:

Microorganism		MIC (mcg/mL)
S. aureus	ATCC 25923	0.25-1.0
E. coli	ATCC 25922	1.0-4.0

INDICATIONS AND USAGE
ANCEF is indicated in the treatment of the following infections due to susceptible organisms:

Respiratory Tract Infections
Due to *S. pneumoniae*, *S aureus* (including β-lactamase–producing strains) and *S. pyogenes*.
Injectable benzathine penicillin is considered to be the drug of choice in treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever.
ANCEF is effective in the eradication of streptococci from the nasopharynx; however, data establishing the efficacy of ANCEF in the subsequent prevention of rheumatic fever are not available.

Urinary Tract Infections
Due to *E. coli, P mirabilis.*

Skin and Skin Structure Infections
Due to *S. aureus* (including β-lactamase–producing strains), *S. pyogenes*, and other strains of streptococci.

Biliary Tract Infections
Due to *E. coli*, various strains of streptococci, *P. mirabilis*, and *S. aureus*.

Bone and Joint Infections
Due to *S. aureus*.

Genital Infections
(i.e., prostatitis, epididymitis) due to *E. coli*, *P. mirabilis.*

Septicemia
Due to *S. pneumoniae*, *S. aureus* (including β-lactamase–producing strains), *P. mirabilis*, *E. coli.*

Endocarditis
Due to *S. aureus* (including β-lactamase–producing strains) and *S. pyogenes.*
Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to ANCEF.

Perioperative Prophylaxis
The prophylactic administration of ANCEF preoperatively, intraoperatively, and postoperatively may reduce the incidence of certain postoperative infections in patients undergoing surgical procedures which are classified as contaminated or potentially contaminated (e.g., vaginal hysterectomy, and cholecystectomy in high-risk patients such as those older than 70 years, with acute cholecystitis, obstructive jaundice, or common duct bile stones).
The perioperative use of ANCEF may also be effective in surgical patients in whom infection at the operative site would present a serious risk (e.g., during open-heart surgery and prosthetic arthroplasty).
The prophylactic administration of ANCEF should usually be discontinued within a 24-hour period after the surgical procedure. In surgery where the occurrence of infection may be particularly devastating (e.g., open-heart surgery and prosthetic arthroplasty), the prophylactic administration of ANCEF may be continued for 3 to 5 days following the completion of surgery.
If there are signs of infection, specimens for cultures should be obtained for the identification of the causative organism so that appropriate therapy may be instituted.
(See DOSAGE AND ADMINISTRATION.)
To reduce the development of drug-resistant bacteria and maintain the effectiveness of ANCEF and other antibacterial drugs, ANCEF should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

CONTRAINDICATIONS
ANCEF IS CONTRAINDICATED IN PATIENTS WITH KNOWN ALLERGY TO THE CEPHALOSPORIN GROUP OF ANTIBIOTICS.

WARNINGS
BEFORE THERAPY WITH ANCEF IS INSTITUTED, CAREFUL INQUIRY SHOULD BE MADE TO DETERMINE WHETHER THE PATIENT HAS HAD PREVIOUS HYPERSENSITIVITY REACTIONS TO CEFAZOLIN, CEPHALOSPORINS, PENICILLINS, OR OTHER DRUGS. IF THIS PRODUCT IS GIVEN TO PENICILLIN-SENSITIVE PATIENTS, CAUTION SHOULD BE EXERCISED BECAUSE CROSS-HYPERSENSITIVITY AMONG BETA-LACTAM ANTIBIOTICS HAS BEEN CLEARLY DOCUMENTED AND MAY OCCUR IN UP TO 10% OF PATIENTS WITH A HISTORY OF PENICILLIN ALLERGY. IF AN ALLERGIC REACTION TO ANCEF OCCURS, DISCONTINUE TREATMENT WITH THE DRUG. SERIOUS ACUTE HYPERSENSITIVITY REACTIONS MAY REQUIRE TREATMENT WITH EPINEPHRINE AND OTHER EMERGENCY MEASURES, INCLUDING OXYGEN, IV FLUIDS, IV ANTIHISTAMINES, CORTICOSTEROIDS, PRESSOR AMINES, AND AIRWAY MANAGEMENT, AS CLINICALLY INDICATED.
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefazolin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.
Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of “antibiotic-associated colitis”.
After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an oral antibacterial drug clinically effective against *C. difficile* colitis.

PRECAUTIONS

General
Prolonged use of ANCEF may result in the overgrowth of nonsusceptible organisms. Careful clinical observation of the patient is essential.
When ANCEF is administered to patients with low urinary output because of impaired renal function, lower daily dosage is required (see DOSAGE AND ADMINISTRATION).

As with other β-lactam antibiotics, seizures may occur if inappropriately high doses are administered to patients with impaired renal function (see DOSAGE AND ADMINISTRATION).
ANCEF, as with all cephalosporins, should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.
Cephalosporins may be associated with a fall in prothrombin activity. Those at risk include patients with renal or hepatic impairment or poor nutritional state, as well as patients receiving a protracted course of antimicrobial therapy, and patients previously stabilized on anticoagulant therapy. Prothrombin time should be monitored in patients at risk and exogenous vitamin K administered as indicated.
Prescribing ANCEF in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Drug Interactions
Probenecid may decrease renal tubular secretion of cephalosporins when used concurrently, resulting in increased and more prolonged cephalosporin blood levels.

Drug/Laboratory Test Interactions

A false positive reaction for glucose in the urine may occur with Benedict's solution, Fehling's solution or with CLINITEST® tablets, but not with enzyme-based tests such as CLINISTIX®.
Positive direct and indirect antiglobulin (Coombs) tests have occurred; these may also occur in neonates whose mothers received cephalosporins before delivery.

Information for Patients

Carcinogenesis/Mutagenesis
Mutagenicity studies and long-term studies in animals to determine the carcinogenic potential of ANCEF have not been performed.

Pregnancy

Teratogenic Effects
Pregnancy Category B. Reproduction studies have been performed in rats, mice, and rabbits at doses up to 25 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to ANCEF. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery
When cefazolin has been administered prior to caesarean section, drug levels in cord blood have been approximately one quarter to one third of maternal drug levels. The drug appears to have no adverse effect on the fetus.

Nursing Mothers
ANCEF is present in very low concentrations in the milk of nursing mothers. Caution should be exercised when ANCEF is administered to a nursing woman.

Pediatric Use
Safety and effectiveness for use in premature infants and neonates have not been established. See DOSAGE AND ADMINISTRATION for recommended dosage in pediatric patients older than 1 month.

Geriatric Use
Of the 920 subjects who received ANCEF in clinical studies, 313 (34%) were 65 years and over, while 138 (15%) were 75 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.
This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function (see PRECAUTIONS, General and DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS
The following reactions have been reported:

Gastrointestinal
Diarrhea, oral candidiasis (oral thrush), vomiting, nausea, stomach cramps, anorexia, and pseudomembranous colitis. Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment (see WARNINGS). Nausea and vomiting have been reported rarely.

Allergic
Anaphylaxis, eosinophilia, itching, drug fever, skin rash, Stevens-Johnson syndrome.

Hematologic
Neutropenia, leukopenia, thrombocytopenia, thrombocythemia.

Hepatic
Transient rise in SGOT, SGPT, and alkaline phosphatase levels has been observed. As with other cephalosporins, reports of hepatitis have been received.

Renal
As with other cephalosporins, reports of increased BUN and creatinine levels, as well as renal failure, have been received.

Local Reactions
Rare instances of phlebitis have been reported at site of injection. Pain at the site of injection after intramuscular administration has occurred infrequently. Some induration has occurred.

Other Reactions
Genital and anal pruritus (including vulvar pruritus, genital moniliasis, and vaginitis).

DOSAGE AND ADMINISTRATION

Usual Adult Dosage

Type of Infection	Dose	Frequency
Moderate to severe infections	500 mg to 1 gram	every 6 to 8 hrs.
Mild infections caused by susceptible gram-positive cocci	250 mg to 500 mg	every 8 hours
Acute, uncomplicated urinary tract infections	1 gram	every 12 hours
Pneumococcal pneumonia	500 mg	every 12 hours
Severe, life-threatening infections (e.g., endocarditis, septicemia)*	1 gram to 1.5 grams	every 6 hours

*In rare instances, doses of up to 12 grams of ANCEF per day have been used.

Perioperative Prophylactic Use
To prevent postoperative infection in contaminated or potentially contaminated surgery, recommended doses are:
a. 1 gram IV or IM administered $^1/_2$ hour to 1 hour prior to the start of surgery.
b. For lengthy operative procedures (e.g., 2 hours or more), 500 mg to 1 gram IV or IM during surgery (administration modified depending on the duration of the operative procedure).
c. 500 mg to 1 gram IV or IM every 6 to 8 hours for 24 hours postoperatively.
It is important that (1) the preoperative dose be given just ($^1/_2$ to 1 hour) prior to the start of surgery so that adequate antibiotic levels are present in the serum and tissues at the time of initial surgical incision; and (2) ANCEF be administered, if necessary, at appropriate intervals during surgery to provide sufficient levels of the antibiotic at the anticipated moments of greatest exposure to infective organisms.
In surgery where the occurrence of infection may be particularly devastating (e.g., open-heart surgery and prosthetic arthroplasty), the prophylactic administration of ANCEF may be continued for 3 to 5 days following the completion of surgery.

Dosage Adjustment for Patients With Reduced Renal Function

ANCEF may be used in patients with reduced renal function with the following dosage adjustments: Patients with a creatinine clearance of 55 mL/min. or greater or a serum creatinine of 1.5 mg % or less can be given full doses. Patients with creatinine clearance rates of 35 to 54 mL/min. or serum creatinine of 1.6 to 3.0 mg % can also be given full doses but dosage should be restricted to at least 8 hour intervals. Patients with creatinine clearance rates of 11 to 34 mL/min. or serum creatinine of 3.1 to 4.5 mg % should be given $^1/_2$ the usual dose every 12 hours. Patients with creatinine clearance rates of 10 mL/min. or less or serum creatinine of 4.6 mg % or greater should be given $^1/_2$ the usual dose every 18 to 24 hours. All reduced dosage recommendations apply after an initial loading dose appropriate to the severity of the infection. Patients undergoing peritoneal dialysis: See CLINICAL PHARMACOLOGY.

Pediatric Dosage

In pediatric patients, a total daily dosage of 25 to 50 mg per kg (approximately 10 to 20 mg per pound) of body weight, divided into 3 or 4 equal doses, is effective for most mild to moderately severe infections. Total daily dosage may be increased to 100 mg per kg (45 mg per pound) of body weight for severe infections. Since safety for use in premature infants and in neonates has not been established, the use of ANCEF in these patients is not recommended.

Pediatric Dosage Guide

Weight		**25 mg/kg/day Divided into 3 Doses**		**25 mg/kg/day Divided into 4 Doses**	
Lbs	Kg	Approximate Single Dose mg/q8h	Vol. (mL) needed with dilution of 125 mg/mL	Approximate Single Dose mg/q6h	Vol. (mL) needed with dilution of 125 mg/mL
10	4.5	40 mg	0.35 mL	30 mg	0.25 mL
20	9.0	75 mg	0.60 mL	55 mg	0.45 mL
30	13.6	115 mg	0.90 mL	85 mg	0.70 mL
40	18.1	150 mg	1.20 mL	115 mg	0.90 mL
50	22.7	190 mg	1.50 mL	140 mg	1.10 mL

Weight		**50 mg/kg/day Divided into 3 Doses**		**50 mg/kg/day Divided into 4 Doses**	
Lbs	Kg	Approximate Single Dose mg/q8h	Vol. (mL) needed with dilution of 225 mg/mL	Approximate Single Dose mg/q6h	Vol. (mL) needed with dilution of 225 mg/mL
10	4.5	75 mg	0.35 mL	55 mg	0.25 mL
20	9.0	150 mg	0.70 mL	110 mg	0.50 mL
30	13.6	225 mg	1.00 mL	170 mg	0.75 mL
40	18.1	300 mg	1.35 mL	225 mg	1.00 mL
50	22.7	375 mg	1.70 mL	285 mg	1.25 mL

In pediatric patients with mild to moderate renal impairment (creatinine clearance of 70 to 40 mL/min.), 60 percent of the normal daily dose given in equally divided doses every 12 hours should be sufficient. In patients with moderate impairment (creatinine clearance of 40 to 20 mL/min.), 25 percent of the normal daily dose given in equally divided doses every 12 hours should be adequate. Pediatric patients with severe renal impairment (creatinine clearance of 20 to 5 mL/min.) may be given 10 percent of the normal daily dose every 24 hours. All dosage recommendations apply after an initial loading dose.

RECONSTITUTION

Preparation of Parenteral Solution

Parenteral drug products should be SHAKEN WELL when reconstituted, and inspected visually for particulate matter prior to administration. If particulate matter is evident in reconstituted fluids, the drug solutions should be discarded.
When reconstituted or diluted according to the instructions below, ANCEF is stable for 24 hours at room temperature or for 10 days if stored under refrigeration (5°C or 41°F). Reconstituted solutions may range in color from pale yellow to yellow without a change in potency.

Single-Dose Vials

For IM injection, IV direct (bolus) injection or IV infusion, reconstitute with Sterile Water for Injection according to the following table. SHAKE WELL.

Vial Size	Amount of Diluent	Approximate Concentration	Approximate Available Volume
1 gram	2.5 mL	330 mg/mL	3.0 mL

Pharmacy Bulk Vials

Add Sterile Water for Injection, Bacteriostatic Water for Injection, or Sodium Chloride Injection according to the table below. SHAKE WELL. Use promptly. (Discard vial within 4 hours after initial entry.)

Vial Size	Amount of Diluent	Approximate Concentration	Approximate Available Volume
10 grams	45 mL	1 gram/5 mL	51 mL
	96 mL	1 gram/10 mL	102 mL

"Piggyback" Vials

Reconstitute with 50 to 100 mL of Sodium Chloride Injection or other IV solution listed under ADMINISTRATION. When adding diluent to vial, allow air to escape by using a small vent needle or by pumping the syringe. SHAKE WELL. Administer with primary IV fluids, as a single dose.

ADMINISTRATION

Intramuscular Administration

Reconstitute vials with Sterile Water for Injection according to the dilution table above. Shake well until dissolved. ANCEF should be injected into a large muscle mass. Pain on injection is infrequent with ANCEF.

Intravenous Administration

Direct (bolus) injection: Following reconstitution according to the above table, further dilute vials with approximately 5 mL Sterile Water for Injection. Inject the solution slowly over 3 to 5 minutes, directly or through tubing for patients receiving parenteral fluids (see list below).
Intermittent or continuous infusion: Dilute reconstituted ANCEF in 50 to 100 mL of 1 of the following solutions:
Sodium Chloride Injection, USP
5% or 10% Dextrose Injection, USP
5% Dextrose in Lactated Ringer's Injection, USP
5% Dextrose and 0.9% Sodium Chloride Injection, USP
5% Dextrose and 0.45% Sodium Chloride Injection, USP
5% Dextrose and 0.2% Sodium Chloride Injection, USP
Lactated Ringer's Injection, USP
Invert Sugar 5% or 10% in Sterile Water for Injection
Ringer's Injection, USP
5% Sodium Bicarbonate Injection, USP

HOW SUPPLIED

ANCEF

Single-Dose Vials
Each vial contains cefazolin sodium equivalent to 1 gram of cefazolin.
NDC 0007-3130-16 (package of 25 vials)

“Piggyback” Vials
Each vial contains cefazolin sodium equivalent to 1 gram of cefazolin.
NDC 0007-3137-05 (package of 10 "piggyback" vials)

Pharmacy Bulk Vials
Each vial contains cefazolin sodium equivalent to 10 grams of cefazolin.
NDC 0007-3135-05 (package of 10 pharmacy bulk vials)
As with other cephalosporins, ANCEF tends to darken depending on storage conditions; within the stated recommendations, however, product potency is not adversely affected.
Before reconstitution protect from light and store at Controlled Room Temperature 20° to 25°C (68° to 77°F).

REFERENCES

1. National Committee for Clinical Laboratory Standards (NCCLS). January 2003. *Performance Standards for Antimicrobial Disk Susceptibility Tests*; Approved Standard - Eighth Edition. NCCLS Document M2-A8 and Disk Diffusion Supplemental Tables M100-S13. NCCLS, Wayne, PA, USA.

2. National Committee for Clinical Laboratory Standards (NCCLS). January 2003. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*; Approved Standard - Sixth Edition. NCCLS Document M7-A6 and MIC Testing Supplemental Tables, M100-S13. NCCLS, Wayne, PA, USA.

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